Application of Molecular Simulation to Prediction of Solubility Parameter

Yoshinori Suga and Tomohiko Takahama
Chemical Science Laboratories, Mitsubishi Chemical Corporation, No.1, Toho-cho, Yokkaichi, Mie 510

(Received December 11, 1995)

Molecular dynamics simulations are performed for six types of solvents to predict the solubility parameters. Investigation of the deciding factor in determining these values is also reported.

Prediction of mixing ability between two solvents is an important issue in terms of scientific aspects and industrial applications. The solubility parameter (δ), first defined by Hildebrand and Scott,[1] has been found to be a useful guide for solvents miscibility. This is defined as the square root of the cohesive energy density.

$$\delta = \left(\frac{\Delta E}{V}\right)^{1/2} = \left(\frac{\Delta H - RT}{V}\right)^{1/2} \qquad (1)$$

where ΔE is the energy of vaporization, V is the molar volume, ΔH is the enthalpy of vaporization, R is the gas constant, and T is the absolute temperature.

The process of dissolving a solute in a solvent is governed by the Gibbs free energy of mixing (ΔGm), which is represented by the enthalpy (ΔHm) and the entropy (ΔSm) change.

$$\Delta Gm = \Delta Hm - T\Delta Sm \qquad (2)$$

Hildebrand and Scott proposed that the enthalpy change can be expressed as

$$\Delta Hm = V'(\delta_1 - \delta_2)^2 \phi_1 \phi_2 \qquad (3)$$

where V' is the volume of mixture, and ϕi is the volume fraction of species i. This equation will be applicable to the mixture with (a) no volume change on mixing at constant pressure, (b) no reaction between the components, and (c) no complex formation or special associations. The entropy of mixing, ΔSm, is always positive so that ΔHm, the enthalpy of mixing, determines whether dissolution occurs or not. Thus, in this model, a good solvent must have a solubility parameter close to, or identical with, that of a solute.

Many theoretical studies of the foundation and the application of this property have been performed.[7,11] However, the microscopic nature has not been clarified in these studies, since they are always based on the group contribution method. In the present paper, we describe the results of molecular simulations for determining solubility parameters using a full atomistic force field.

In our simulations the solvent molecules were described by the interaction potentials developed by Maple and co-workers[2] (CFF91), as having a, three, and four body nature, allowing respectively for stretch, bending, torsional, and out-of-plane motions. They also have additional cross terms, which represent coupling interactions (e.g., angle/torsion coupling interactions). For nonbond interactions, the Lennard-Jones and electrostatic terms that play the most important role in the cohesive energy calculation, are included. With regard to the detail, the reader should refer to the literature [2].

The simulation cell contained one hundred molecules, as in Figure 1, and was constructed to satisfy the experimental density.[3] This was periodically replicated in all directions. Molecular dynamics (MD) calculations were carried out for each structure using the leap-frog algorithm[4] with a time step of 1.0 fs under NVT conditions (T=298 K). Temperatures were stabilized with scaling the atomic velocities.[4] Potential energies were truncated at 10.0 Angstrom, and the Ewald method[5] was taken to calculate cohesive energies. All simulations were performed with molecular modeling package, InsightII, Discover, and Amorphous Cell, as supplied by BIOSYM Technologies Inc.[2]

Figure 2 shows the time evolution of the total potential energy of the liquid benzene. It is clear that the duration (50ps) is valid to make the system equilibrium. We averaged the cohesive energies for twenty structures after the MD run described above. As in Table 1, we confirmed that the calculated results were in agreement with the experimental values quantitatively. Therefore, in the case when MD calculation is executed with an accurate forcefield, such as CFF91, it should be possible to predict a solubility parameter from an atomistic simulation.

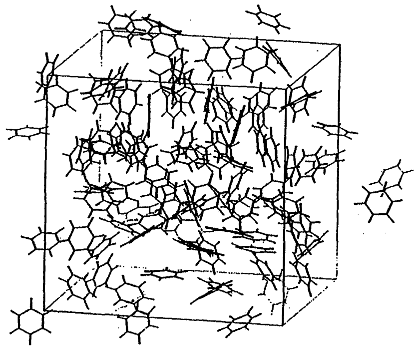

Figure 1. Image of a simulation cell which contained one hundred benzene molecules.

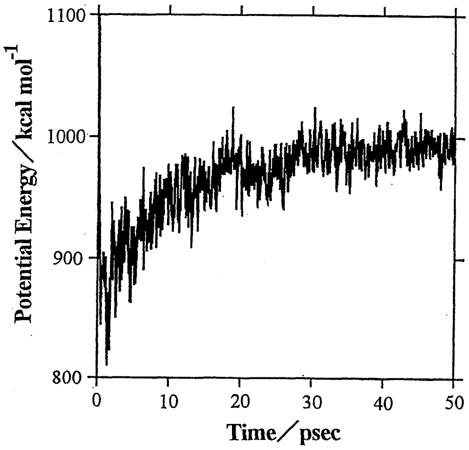

Figure 2. Plot of total potential energy (1 cal = 4.184 J) vs. time, obtained from the system, as in Figure 1.

Table 1. Solubility parameters of solvents at 298 K

	Solubility Parameter/MPa$^{1/2}$			
Solvent	calc.[a]	calc.[b]	exp.[c]	exp.[d]
n-Pentane	14.9	5.9	14.5	14.3
n-Octane	15.7	6.3	15.5	15.6
Benzene	18.7	8.4	18.6	18.8
Toluene	18.2	7.5	18.2	18.2
Pyridine	21.6	8.8	21.8	21.9
Acetone	19.8	9.5	20.0	20.3

[a] Calculations are carried out with the three dimensional periodic cell mimicking the liquid state. [b] Determined by the cluster formation energy. [c] Reference 3. [d] Reference 10.

Table 2. Dispersion force contribution to the total solubility parameters of solvents at 298 K

	Solubility Parameter[a] /MPa$^{1/2}$	
Solvent	δd(This Work)	δd(Hansen[b])
n-Pentane	14.9 (1.00)	14.5 (1.00)
n-Octane	15.6 (0.99)	15.5 (1.00)
Benezene	17.9 (0.96)	18.4 (0.99)
Toluene	17.8 (0.98)	18.0 (0.99)
Pyridine	18.4 (0.85)	19.0 (0.87)
Acetone	18.0 (0.91)	15.5 (0.78)

[a] The ratios of dispersion force contribution to the total solubility parameter are shown in parentheses. [b] References 3,7.

A further study was done on the effect of van der Waals interaction to the total solubility parameter. Hansen[7] proposed an extension of this parameter, which could be split as the following equation shows:

$$\delta^2 = \delta_d^2 + \delta_a^2 \qquad (4)$$

where δd is the dispersion force contribution, and δa is the dipole and the hydrogen bonding one. A comparison between the calculated van der Waals interaction and the Hansen's parameter are listed in Table 2. Interestingly, the large difference was observed in the acetone case. Considering the reason for this large discrepancy, one can suspect the accuracy of the CFF91 forcefield. However, this would be contradicted as the total solubility parameter and the dipole moment (μ=2.63 Debye) calculated with this forcefield reasonably agree with its experimental values[8] (μ=2.88 Debye). It may be concluded that the Hansen's parameter for acetone has a problem in the rate of dispersion force contribution.

In order to investigate the deciding factor in determining the solubility parameter value, we calculated the formation energies of two molecular clusters, which was the structure composed of two identical molecules being associated with its intermolecular forces in vacuum. The cluster was obtained with energy minimization after the randomly orienting two molecules that were picked from the trajectory of MD run for the single molecule. We averaged 500 structures to get statistically certain results. The values were transformed to the energy per unit volume to compare the solubility parameters. This method, named FLEXIBLEND, was proposed by Tiller.[9]

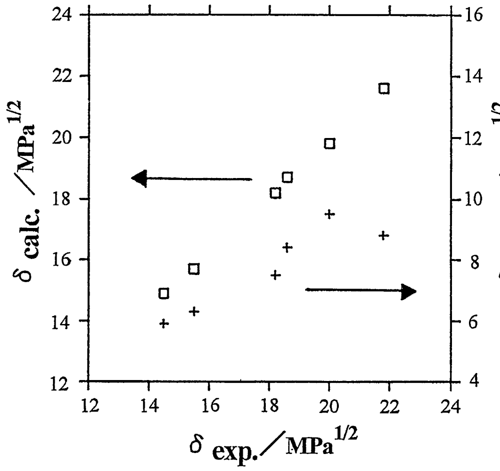

Figure 3. Plot of calculated solubility parameters vs. experiments. Obtained from the system, as the liquid structure (□), and the cluster structure (+).

The results are shown in Table 1 and Figure 3. What is evident from the table is the cohesive energies, calculated from the cluster formation, which have the ability to predict the qualitative trend of the solubility parameters on the whole. In other words, the short range interaction between two molecules would play the essential role in determining these values. The averaged ratio of solubility parameters, that of cluster formation and liquid calculation, is 0.43. We think the variety of these ratios will come from the differences in coordination numbers for each solvent.

In conclusion, we investigated the quantitative prediction of a solubility parameter with atomistic simulation, which is possible if we used an accurate forcefield. Studying the contribution of dispersion force to the total solubility parameter, we found the estimation of Hansen's parameter might be a problem in the acetone case. We have also reported that the cluster formation energies of two identical molecules would be enough to get a rough prediction of them.

References and Notes

1 J. Hildebrand and R. L. Scott, The Solubility of Nonelectrolytes, Rheinhold, New York (1950).
2 J. R. Maple, M. J. Hwang, T. P. Stockfisch, U. Dinur, M. Waldman, C. S. Ewig, and A. T. Hagler, *J. Comput. Chem.*, **15**, 162 (1994).
3 A. F. M. Barton, CRC Handbook of Solubility Parameters and Other Cohesion Parameters, CRC Press (1983).
4 M. P. Allen and D. J. Tildesley, Computer Simulation of Liquids, Clarendon Press, Oxford (1987).
5 M. P. Tosi, *Solid State Physics*, **16**, 107 (1964).
6 BIOSYM Technologies Inc., 9685 Scranton Road, San Diego, CA.
7 C. M. Hansen, *J. Paint. Techn.*, **39**, 104 (1967).
8 CRC Handbook of Chemistry and Physics, 73rd ed, ed by D. R. Lide, CRC Press (1992).
9 A. R. Tiller and B. Gorella, *Polymer*, **35**, 3251 (1994).
10 Polymer Handbook, 3rd ed, ed by J. Brandrup and E. H. Immergut, VII/519, Wiley (1989).
11 P. L. Huyskens and M. C. Haulait-Pirson, *J. Coat. Techn.*, **57**, 57 (1985).